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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,894	04/20/2001	Zeev Alboum	UOFMD.006A	4293
23373	7590	10/21/2003	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. WASHINGTON, DC 20037			LUCAS, ZACHARIAH	
			ART UNIT	PAPER NUMBER

1648

DATE MAILED: 10/21/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/839,894

Applicant(s)

ALTBOUM ET AL.

Examiner

Zachariah Lucas

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 82-93 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 82 and 84 is/are allowed.
- 6) ☒ Claim(s) 83 and 85-93 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 82-93 are pending in the application. Claims 1, 12-16, 35, and 48-50 were pending and rejected in the prior action, mailed on February 11, 2003. These claims were cancelled and replaced by new claims 82-93 in the Response filed on August 7, 2003.
2. In view of the new rejection raised in this action, the action is being made Non-Final.

### ***Specification***

3. **(Prior Objections-Withdrawn)** The disclosure was objected to in the office action mailed July 30, 2002 (the prior action) for various informalities. In view of the amendments made to the specification in the response filed November 26, 2002 (Amend. A), the objections are hereby withdrawn.

### ***Drawings***

4. **(Prior Objection-Withdrawn)** In the prior action, the proposed corrections for Figures 2A and 2B were approved by the examiner with respect to the subject matter enclosed therein. In view of the submission of the formal corrected version of Figure 2 on August 7, 2003, the objection is withdrawn.

### ***Claim Objections***

5. **(New Objection- Necessitated by Amendment)** Claims 92 and 93 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject

Art Unit: 1648

matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims read on combination of a substantially pure CsaE polypeptide in combination with a substantially pure CsaB polypeptide or CS4 polypeptide. However, the Applicant indicated in the Response that the substantially pure language in the claims was intended to exclude the combination of the CsaE antigen with the CsaB antigen, which, together, dimerize to form CS4. As the substantially pure language excludes the presence of other ETEC antigens, the dependant claims indicating the presence of such other antigens is not further limiting of the claimed invention as the further limitations are inconsistent with the substantially pure language.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **(New Rejection- Necessitated by Amendment)** Claims 85-93 as added are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on substantially pure polypeptides resulting from recombinant expression of a polynucleotide that hybridizes under high stringency conditions with the polynucleotide of SEQ ID NO: 9. However, the Applicant has not defined what is meant by the phrase “high stringency conditions.” While the Applicant has provided examples of what may be a high stringency condition, there is no definition by which one of ordinary skill could determine the scope of conditions that the Applicant considers to fall within the phrase. If those in the art cannot

Art Unit: 1648

determine what is meant by high-stringency conditions, they also would not be able to determine the range of polynucleotides included by the claim language. Because the scope of such conditions affects the scope of the claims, absent a definition for the phrase, the claim is indefinite.

8. **(New Rejection- Necessitated by Amendment)** Claims 86-93 as added are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on an immunogenic composition comprising a substantially pure CsaE protein in combination with a substantially pure CsaB protein or CS4 antigen. In the Response to the anticipation rejection over the McConnell and Rudin, the Applicant argued that “in view of the ‘substantially pure’ language in the claims, Applicants are reciting a CsaE polypeptide free of other naturally occurring components, such as the CsaB polypeptide.” Response, page 7. In view of this language clearly indicating that the phrase “substantially pure” excludes the presence of other ETEC antigens, including CsaB, the subject matter of claims 92 and 93, which includes both the CsaE and CsaB antigen is inconsistent with the language of the claims from which they depend. In view of the inconsistency of the claims and the statements by Applicant as to the meaning of the claims, the scope of the identified claims is rendered indefinite.

9. **(Prior Rejection- Withdrawn)** Claims 1, and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

Art Unit: 1648

subject matter which applicant regards as the invention. In view of the cancellation of these claims, the rejection is withdrawn.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. **(New Rejection)** Claims 83, and 85-93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a CsaE polypeptide comprising SEQ ID NO: 10, does not reasonably provide enablement for any polypeptide that is at least 95% homologous thereto. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claim 83 reads on substantially pure polypeptides with amino acids sequences at least 95% homologous to SEQ ID NO: 10. Claim 85 reads on polypeptides encoded by DNAs that hybridize to the complement of SEQ ID NO: 9. Such polypeptides would appear to include full-length homologues of SEQ ID NO: 9, and fragments thereof. Claims 85-93 read on immunogenic compositions comprising any of the polypeptides of claims 83 or 85. Thus, the claims read broadly on the polypeptide of SEQ ID NO: 10, homologues of the protein, and fragments thereof.

The Examiner concedes that those in the art would be capable of making the claimed polypeptides and fragments. However, there are insufficient teachings in the application to enable one in the art to use any homologue or fragment of the claimed invention. The claims do not require that the claimed polypeptides have any particular function, and the specification

Art Unit: 1648

provides no examples of fragments or homologues of either SEQ ID NO: 10 or 9. Further, the specification provides no identification of any functional regions or epitopes on the protein of SEQ ID NO: 10.

In combination with the lack of guidance to useful homologues and fragments of the CsaE polypeptide, the art teaches that the effect of modification of proteins is unpredictable. See e.g., Bowie et al., Science 247: 1306-10, at 1306 (indicating that the effects of even conservative substitutions is unpredictable absent information about the importance of the modified residue to protein function and/or structure). See also, Abaza et al., J Prot Chem 11: 433-44; and Riffkin et al., Gene 167: 279-83 (each teaching that a single amino residue substitution in a protein can change its immunogenic properties, even where the substitution is outside the antigenic region). Thus, in view of the limited information in the specification regarding the epitopic and functional sites in the CsaE protein, and the unpredictability of the art, the Applicant has not provided sufficient information to enable one skilled in the art to both make, and to use, the claimed inventions.

12. **(New Rejection- Necessitated by Amendment)** Claims 85-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make, and/or use the invention. The claims read substantially pure CsaE polypeptides encoded by the expression of polynucleotides that hybridize to SEQ ID NO: 9. The Applicant has disclosed SEQ ID NO: 9 as encoding CsaE polypeptides. See e.g., claim 84. Because SEQ ID NO: 9 encodes a

Art Unit: 1648

CsaE polypeptide, and because the complementary strand (or hybridization partner) thereof would inherently not encode the same polypeptide, the Applicant is not enabled for CsaE polypeptides encoded by such a polynucleotide.

13. **(Prior Rejection- Withdrawn** Claim 16 was rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In view of the cancellation of this claim, the rejection is withdrawn.

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. **(Prior rejection –Withdrawn)** Claims 1, 10-11, 35, and 48-50 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by McConnell et al., Infection and Immunity, 56:1974-1980 (McConnell), and Rudin et al, Microbial Pathogenesis, 16:131-139 (Rudin). In view of the amendment to claim 1, the rejection is withdrawn from this claim. As claims 10-11, 35, and 48-50 have been cancelled from the application, the rejection of these claims is withdrawn. Further, as claims 82-85 each read on only a substantially pure CsaE polypeptide, the rejection is not extended to these claims.



Art Unit: 1648

Because the references do not teach the incorporation of only the CS4 pili into an immunogenic composition, the rejection is not extended to new claims 86-93, in favor of the new obviousness rejection below.

16. **(Prior Rejection –Withdrawn)** Claims 1, 12-15, and 35 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by WO 96/38171, naming Cassels et al. as inventors (Cassels). In view of the amendments to the claims, and the Applicant's arguments, the rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. **(Prior Rejection –Maintained over new claims)** Claims 12-15 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over McConnell in view of Cassels. Claims 12-15 have been cancelled from the Application. However, new claims 86-93 read on substantially similar subject matter. While it is noted that the new claims read on a combination of "substantially pure" polypeptides, in view of the indefiniteness of the claims, the rejection of claims 12-15 over McConnell and Cassels is maintained over the new claims. From the teachings of McConnell, one of ordinary skill in the art would have been capable of purifying the CS4 antigen. As it is unclear whether or not the term "substantially pure" would include the combined

Art Unit: 1648

antigens of CsaE and CsaB, in view of the open language (“comprising”) the claims are being read as including the isolated dimer of the two proteins. (See also, attached Requirement for Information). The rejection is therefore extended to, and maintained over, new claims 86-93.

### **Requirement for Information**

19. Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

The Applicant has indicated that the CS4 antigen is a dimer of the CsaE and the CsaB proteins. The Applicant has also claimed a composition (claim 86-93) comprising both of these proteins in “substantially pure” forms. In view of this, and the outstanding rejection regarding the claims based on the teachings of McConnell (teaching the CS4 antigen), information regarding the ability of the CsaE and CsaB proteins to autonomously recombine is relevant to the Office’s consideration of the McConnell reference as prior art to the claimed invention. The Office therefore requires any information known to Applicant regarding whether the dimerization of the substantially pure CsaE and CsaB proteins would occur autonomously to form the CS4 antigen.

20. The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained will be accepted as a complete reply to the requirement for that item.

Art Unit: 1648

***Conclusion***

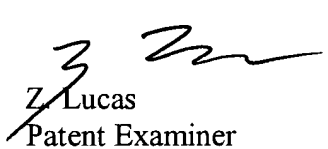
21. Claims 82 and 84 appear to be allowable.


22. **This Office action includes a requirement for information under 37 CFR 1.105.** A complete reply to this Office action must include a complete reply to the attached requirement for information. The time-period for reply to the attached requirement coincides with the time-period for reply to this Office action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Z. Lucas  
Patent Examiner  
October 20, 2003

  
JAMES HOUSEL 10/20/03  
SUPERVISORY PATENT EXAMINER  
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